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Document Number 1

Entry 1 of 961 File: USPT Mar 14, 2000

US-PAT-NO: 6037329
DOCUMENT-IDENTIFIER: US 6037329 A
TITLE: Compositions containing nucleic acids and ligands for therapeutic treatment
DATE-ISSUED: March 14, 2000
US-CL-CURRENT: 514/44; 424/93.21, 435/320.1, 435/325, 435/455, 435/458, 435/69.1, 530/350, 536/23.1
APPL-NO: 8/ 718904
DATE FILED: September 24, 1996
PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS The application is a continuation-in-part of U.S. application Ser. No. 08/441,979, filed May 16, 1995, now abandoned; which is a continuation-in-part of U.S. application Ser. No. 08/213,446, filed Mar. 15, 1994, now abandoned; Ser. No. 08/213,447, filed Mar. 15, 1994, now abandoned; Ser. No. 08/297,961, filed Aug. 29, 1994, now abandoned; and Ser. No. 08/305,771, filed Sep. 13, 1994, now abandoned.

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Document Number 6

Entry 6 of 961 File: USPT Mar 14, 2000

DOCUMENT-IDENTIFIER: US 6036955 A
TITLE: Kits and methods for the specific coagulation of vasculature

BSPR:
Alternatively, such bispecific coagulating agents may be fusion proteins prepared by molecular biological techniques, i.e., by joining a gene (or cDNA) encoding a binding ligand or region to a gene (or cDNA) encoding a coagulation factor. This is well known in the art and is further described herein. Typically, an expression vector is prepared that comprises, in the same reading frame, a DNA segment encoding the first binding region operatively linked to a DNA segment encoding the coagulation factor and expressing the vector in a recombinant host cell so that it produces the encoded fusion protein.

DEPR:
In general, to prepare a fusion a protein one would join a DNA coding region, such as a gene or cDNA, encoding a binding ligand or other targeting region to a DNA coding region (i.e., gene or cDNA) encoding a coagulation factor or coagulant binding region. This typically involves preparing an expression vector that comprises, in the same reading frame, a first DNA segment encoding the first binding region operatively linked to a second DNA segment encoding the coagulation factor. The sequences are attached in a manner such that translation of the total nucleic acid yields the desired bispecific compounds of the invention. Expression vectors contain one or more promoters upstream of the inserted DNA regions that act to promote transcription of the DNA and to thus promote expression of the encoded recombinant protein. This is the meaning of "recombinant expression".

Document Number 114

Entry 114 of 961 File: USPT Nov 2, 1999

DOCUMENT-IDENTIFIER: US 5977307 A
TITLE: Transferrin receptor specific ligand-neuropharmaceutical agent fusion proteins

DEPR:
The ligand-neuropharmaceutical agent fusion protein, which has both ligand binding and neuropharmaceutical characteristics, can be produced as a contiguous protein by using genetic engineering techniques. Gene constructs can be prepared comprising DNA encoding the ligand fused to DNA encoding the protein, polypeptide or peptide to be delivered across the blood brain barrier. The ligand coding sequence and the agent coding sequence are inserted in the expression vectors in a suitable manner for proper expression of the desired fusion protein. The gene fusion is expressed as a contiguous protein molecule containing both a ligand portion and a neuropharmaceutical agent portion. For example, sequences encoding neurotrophic agents such as NGF (nerve growth factor) or CNTF (ciliary neurotrophic factor) can be fused with the sequence encoding transferrin to create chimeric polypeptides that will be expressed and subsequently transported across the BBB via the transferrin receptor.

DEPR:
The genetic engineering techniques are often used to insert linker DNA sequences between the ligand and the neuropharmaceutical agent DNA encoding sequences. These linker DNA sequences can be expressed as part of the fusion protein. For example, specific segments of the constant region of an antibody, including the hinge region, can be inserted between the ligand and the neuropharmaceutical agent. These expressed insertions serve to separate the ligand from the neuropharmaceutical agent and may facilitate the proper folding of the expressed ligand or agent into its proper conformation. When the insertions are segments from the constant region of antibodies that are syngeneic to the host, they have the added advantage of having reduced immunogenicity when administered.

DEPR:
Such chimeric antibodies can readily be adapted to being part of the fusion proteins of this invention. The DNA which contains the variable region coding sequence can be fused to DNA which contains the neuropharmaceutical agent coding sequence for subsequent expression as a fusion protein. Likewise, the DNA which contains the variable region coding sequence can be fused to DNA which contains the coding sequence of a second ligand, if such an expressed fusion protein is desired. The chimeric antibodies comprising constant and variable region portions from two different species can easily be converted to fusion proteins of this invention by inserting DNA encoding a neuropharmaceutical agent or DNA encoding another ligand after a specific portion of constant region encoding DNA. The subsequently expressed fusion protein will then contain the variable region from one species, a desired portion of the constant region from another species and a second ligand or the agent to be transferred across the blood brain barrier.